The University of Chicago

THE CONDENSATION OF 2-METHYLBUTENAL WITH CITRAL

A DISSERTATION SUBMITTED TO THE FACULTY OF THE DIVISION OF THE PHYSICAL SCIENCES IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
1938

By
HENRY M. WALTON

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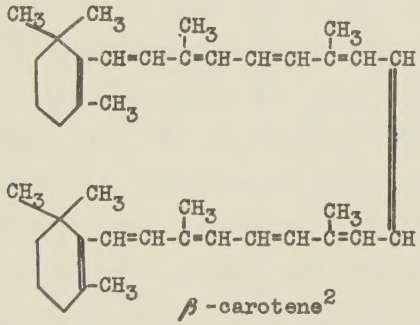
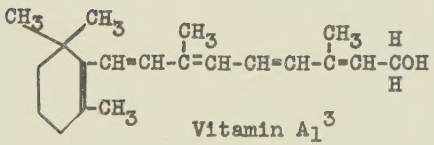
THE CONDENSATION OF 2-METHYLBUTENAL WITH CITRAL

Introduction

Carotinoids may be defined as nitrogen-free polyene pigments consisting wholly or chiefly of long acyclic chains of carbon atoms united in an uninterrupted sequence of conjugated double bonds. Ever since Karrer established the structures of β-carotene and vitamin A_1,[1] numerous attempts have been made to synthesize carotinoids, notably the vitamin.



β-carotene[2]



Vitamin A_1[3]

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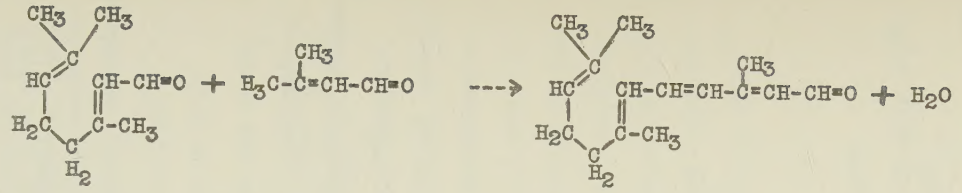
[1] On vitamin A_2, see Heilbron et al., Biochem. J., 32, 405 (1938).

[2] In α- and γ-carotene, one β-ionone ring of β-carotene is replaced by an α-ionone ring and an open chain configuration respectively. The structure of δ-carotene is not yet known.

[3] Vitamin A_1 can be formed by hydrolytic scission of carotene in the animal body.

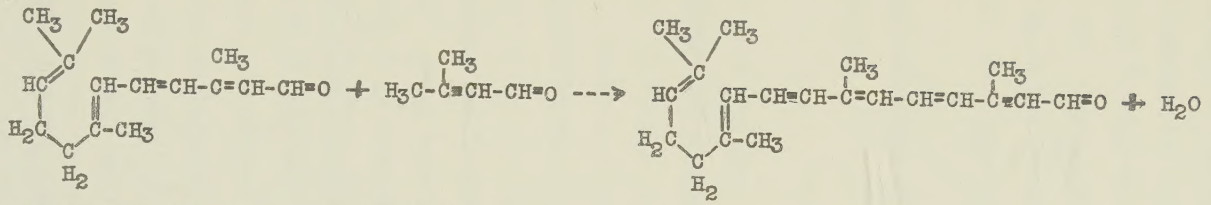
Thus far these attempts have been unsuccessful, save for Kuhn's synthesis of vitamin A_1, which we shall consider shortly. The chief difficulty lies in the construction of long chains of conjugated double bonds carrying methyl side-chains in definite positions. The solution of this problem will probably involve the repeated use of 2-methylbutenal or of substances resulting from its self-condensation.[4] However, since carotinoids are less unsaturated in their terminal carbon configurations than substances resulting from the self-condensation of 2-methylbutenal alone, other more highly saturated cyclic or acyclic aldehydes will have to be condensed with this aldehyde. Citral would appear to be a suitable aldehyde. The method shown by the following equations represents a possibility of building up vitamin A_1 on the basis of the principle indicated. It should be noted that citral is a mixture of two isomers differing by having an isopropylidene and isopropylene configuration, respectively, in their hydrocarbon ends (terpinolene and limolene forms). The isopropylidene configuration predominates. The substances resulting from the following reactions will probably consist of analogous mixtures.

I.



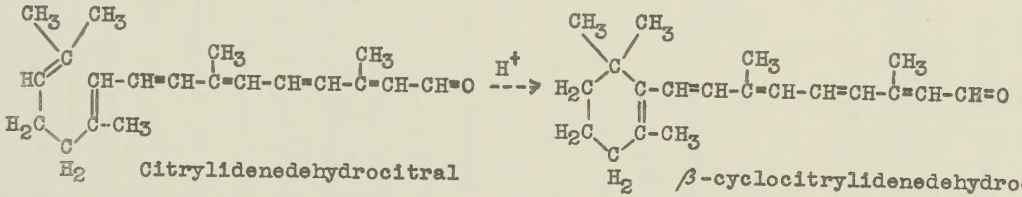
Citral 2-Methylbutenal Dihydrofarnesinal

II.



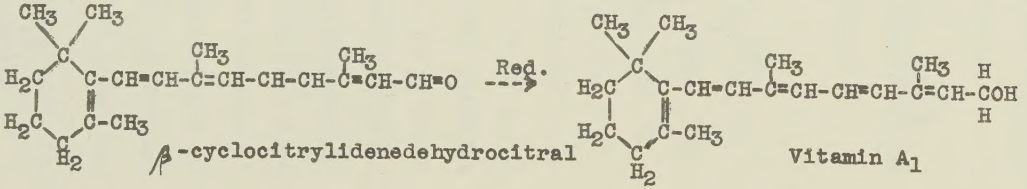
Dihydrofarnesinal 2-Methylbutenal Citrylidenedehydrocitral

III.



Citrylidenedehydrocitral β-cyclocitrylidenedehydrocitral

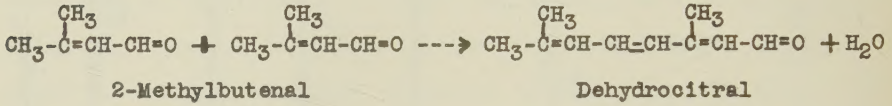
IV.



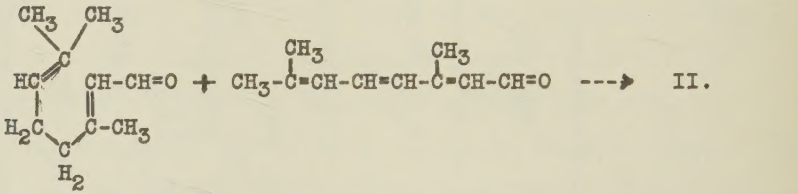
β-cyclocitrylidenedehydrocitral Vitamin A_1

Berhauer and collaborators have proposed a synthesis of the product in II, involving the condensation of citral with 2,6-dimethyloctatrienal.[6] They were unable to prepare the desired substance, and although it was prepared later,[7] the exact conditions of the process have not yet been published. For reasons to be discussed later this approach does not appear to be very promising.

An alternate plan is indicated below. In both of these



2-Methylbutenal Dehydrocitral



Citral Dehydrocitral

schemes, ring closure and reduction of the carbonyl group can probably be carried out in the reverse order. If the ring closure is already carried out with the product of I, β-ionylideneacetaldehyde would result, which can subsequently condense with another mole of 2-methylbutenal to yield the product of III, which may be treated as in IV. This plan was proposed by Heilbron and Jones[8] in October 1936, who claimed, without giving details, to have carried out the first two steps; but nothing has since been published to substantiate this claim. Fuson and Christ[9] attempted

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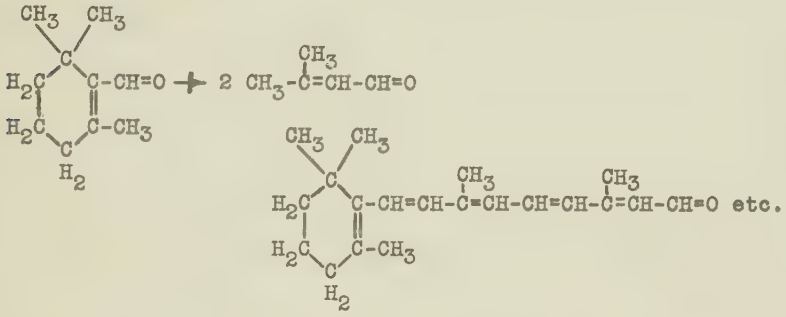
[6]Bernhauer et al., Biochem. Z., 249, 199 (1932).

[7]Fischer and Löwenberg, op. cit.

[8]Heilbron and Jones, Chem. and Ind., 814 (1936).

[9]Fuson and Christ, Science, 84, 294 (1936).

to condense β-cyclocitral with two moles of 2-methylbutenal to form the aldehyde corresponding to vitamin A_1, and to reduce this aldehyde to the vitamin. The mixture which they obtained produced



a blue coloration with antimony trichloride in chloroform, and showed an adsorption band at 328 mμ. This behavior, however, is not characteristic of vitamin A_1 alone, and, in the absence of biological tests, would not constitute satisfactory evidence of the formation of the vitamin. Indeed, although the cyclocitrals condense with acetone to form ionones, β-cyclocitral seems to be reluctant to condense with aldehydes, particularly with unsaturated aldehydes.[10]

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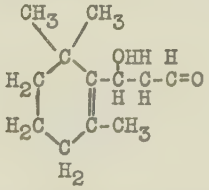
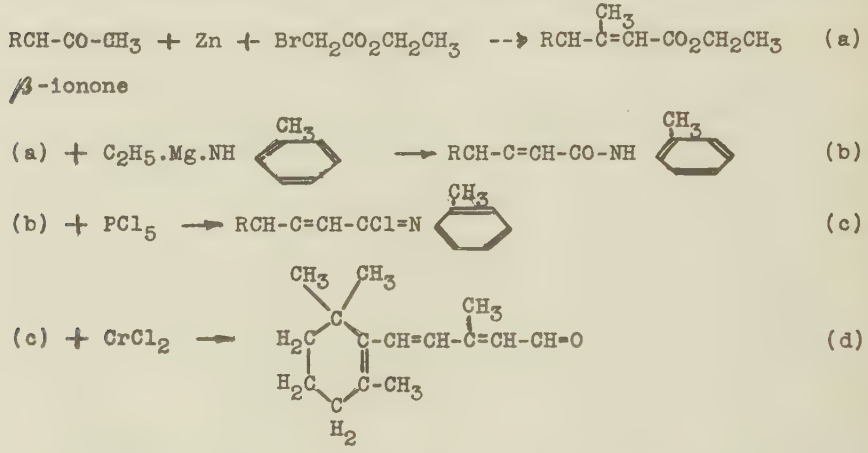
[10] Heilbron and Jones, op. cit. Condensation of β-cyclocitral yielded mainly an aldol which resisted dehydration and which, according to spectrographic evidence, could not have the structure



With crotonaldehyde a mixture was obtained which gave a blue coloration with the antimony trichloride reagent, but the same color test is given by crotonaldehyde self-condensation mixtures.

Two attempts have been made to synthesize β-ionylideneacetaldehyde without the use of 2-methylbutenal. Heilbron's attempt to arrive at it by heating the calcium salt of the corresponding acid with calcium formate was unsuccessful, whereas Kuhn and Morris succeeded in preparing the aldehyde, starting from β-ionone.[11] The ionone, after purification through its semicarbazone, was treated with zinc and bromoacetic ester, and the resulting ester was next converted into the corresponding orthotoluidide, which was reduced to the aldehyde by von Braun's chromous chloride method. Kuhn and Morris, through condensation



with 2-methylbutenal and subsequent reduction of the resulting aldehyde (which was not isolated) arrived at a 7.5 per cent concentration of the vitamin. It would appear that the method described does not lend itself to preparations on a larger scale.

In saturated aldehydes, hydrogen atoms "alpha" to the carbonyl group are labilized, and, in the presence of a suitable aldehyde, may attach themselves to the carbonyl group of the latter with the formation of a new bond between the alpha carbon atom of

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[11] Kuhn and Morris, Ber., 70, 826 (1937).

the donor and the carbonyl carbon atom of the acceptor molecule. Thus an aldehyde possessing both functions may undergo self-condensation. In unsaturated aldehydes the "alpha" effect is transmitted through a system of double bonds conjugated with the carbonyl group. Crotonaldehyde[12] and 2-methylbutenal[13] are capable of self-condensation, and crotonaldehyde has been condensed, through its γ-carbon atom, with citral.[14]

In order to understand the possible course of the aldol condensations studied here (I, II), both the donor and the acceptor functions of the aldehydes in questions must be considered. Although the alpha effect is transmitted, it is subject to modifications by other factors. It is weakened with the increasing length of the chain of conjugated double bonds. Thus, although sorbic aldehyde and octatrienal readily undergo the typical carbonyl reactions, including condensation with acet- and crotonaldehydes, the ability to undergo self-condensation reactions is greatly diminished in sorbic aldehyde and extinct or negligible in octatrienal.[15] The acceptor function of unsaturated aldehydes, too, is weakened with increasing chain length, but to a much lesser extent.[16] The course of crossed aldol condensations of unsaturated aldehydes will therefore primarily depend on the relative "donor" capacities of the aldehydes.[17] In the proposed condensations of

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[12] Fischer and Hultzsch, Ber., 79, 370 (1937).

[13] See p. 1.

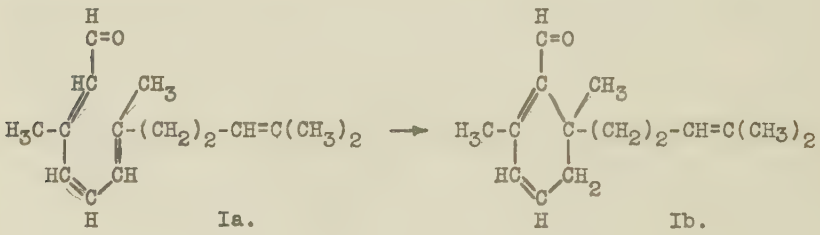
[14] Heilbron et al., J. Chem. Soc. London., 855 (1937).

[15] Fischer and Hultzsch, Ber., 70, 1726 (1937).

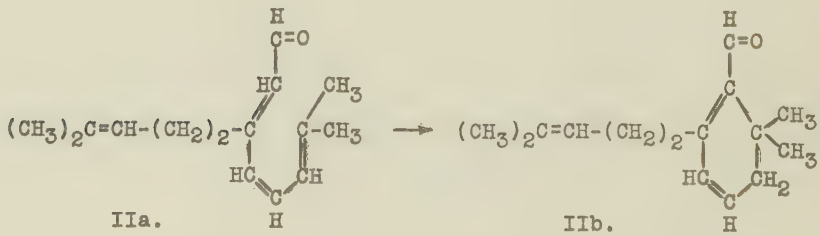
[16] Kuhn and Grundmann, Ber., 70, 1326 (1937).

[17] In analogy to octatrienal the "donor" function of dehydrocitral may be assumed to be extinct. This aldehyde, therefore, is unsuitable for the condensation with citral as proposed by Bernhauser (see p. 6).

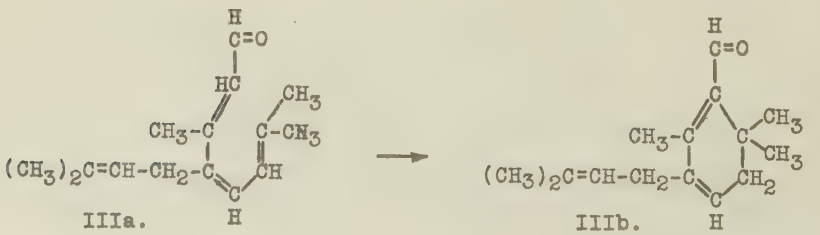
citral and 2-methylbutenal the same phenomena are to be expected. On this basis it may be predicted that dihydrofarnesinal (II) and 2-methylbutenal will condense through a γ-carbon of the lower aldehyde predominantly if not exclusively. No such definite prediction can be made for the interaction of citral and 2-methylbutenal. The configuration involved in aldol condensations is essentially the same in both aldehydes, with an isoamylene group substituted for one of the γ-hydrogen atoms of 2-methylbutenal. The donor and the acceptor functions of the two aldehydes probably do not differ sufficiently to exclude condensation reactions of the carbonyl groups of either aldehyde. The products of the following formulas may result:



Ia. Ib.



IIa. IIb.



IIIa. IIIb.

Compounds Ib, IIb, and IIIb may result, if subsequent ring closure occurs, as happens under certain conditions during the self-condensation of crotonaldehyde.[18]

Thus far we have considered only aldol condensations between citral and 2-methylbutenal. It need not be mentioned that self-condensation of both aldehydes may take place simultanesously.

However, the interaction of the aldehydes is not restricted to the aldol type of condensation. Ring compounds may be formed by Diels-Alder condensation between the normal and the enolized form of the aldehydes. This type of reaction predominates in the presence of sodium amide in ether, but seems to occur to some extent under quite different conditions also.[19]

Reactions I and II pertain not only to the synthesis of vitamin$_1$, but to the possible synthesis of a whole series of carotinoids. Methods are available to convert aldehydes, with loss of their carbonyl oxygen, into the corresponding dialkylidene or "polyenylidene" compounds.[20] Pinacol reduction would join the two aldehydes at their carbonyl carbon atoms, phosphorus diiodide would subsequently remove two hydroxyl groups. Alternately, the aldehydes may be converted into the unstable thio, or seleno, aldehydes, which tend to stabilize themselves by the loss of sulfur, or selenium, and junction of the residues. From reaction II lycopene could be obtained. Likewise, the aldehyde obtained in reaction III could be further condensed with 2-methylbutenal. β-cyclocitrylidenedehydrocitral would yield β-carotene. A mixture

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[18] Bernhauer, op. cit.

[19] This has been observed by Fischer and Löwenberg, op. cit., for 2-methylbutenal as well as for citral. See also Fischer and Hultzsch, Ber., 68, 1730 (1935), on monocyclic C_{15} aldehyde from 2-methylbutenal.

[20] Developed mainly by Kuhn and Winterstein. See Kuhn, J. Chem. Soc., London, 608 (1938).

of the α- and β-isomers of the aldehyde might result in the formation of α-carotene. It might simultaneously lead to the formation of a carotene, not found in nature, containing two α-ionone rings. Likewise, a mixture of the aldehyde and the product of reaction II, might produce γ-carotene in addition to lycopene, et cetera.

The stereochemistry of carotinoids and of compounds containing long chains of conjugated double bonds in general offers problems which are not at all solved. Because of energy relations, the number of cis-trans configurations actually capable of existence is undoubtedly much smaller than that allowed for by merely geometrical considerations. The solid carotinoids, with a few exceptions,[21] have the trans-trans configurations. On the other hand, there is good reason to assume that vitamin A_1, as usually obtained, is a mixture of stereoisomers.[22] The diphenylpolyenes, prepared by Kuhn and his collaborators, are obtained in the trans-trans configuration only. But this result is probably to be ascribed to the method of preparation rather than to the instability of other configurations.[23] It has been shown that methyl side-chains attached to conjugated double bond systems promote the formation and stability of configurations other than trans-trans.[24]

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[21] Cis-crocetin, bixin-(cis).

[22] Holmes and Corbet, J. Am. Chem. Soc., 59, 2042 (1937), claim to have crystallized vitamin A_1, m.p. 6°. It is usually obtained as a pale yellow oil. Heilbron et al., J. Chem. Soc., London, 176 (1938), have been unable to effect a crystallization of the vitamin. Related polyene aliphatic alcohols have high melting points (octatrienol m.p. 122-24°, dodecapentaenol m.p. 204°, farnesinol m.p. 136-37°, and even β-cyclocitral has a melting point of 43-44°.

[23] Kuhn and Winterstein, Ber., 63, 3176 (1930).

[24] Kuhn and Hoffer, Ber., 65, 651 (1932).

More recently, spontaneous isomerization of lycopene, as well as the interconversion of alpha and beta carotenes, have been observed and this has demonstrated that the stereochemical configurations of carotinoids are not as stable as has long been believed.[25] We therefore have to expect that compounds I and II will be obtained as a mixture of stereoisomers.[26]

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[25] Zechmeister and Tuzson, Nature, 141, 249 (1938). See also Zechmeister and Cholniky, Ann., 530, 291 (1937).

[26] Another form of isomerism, probably occurring among the substances of this mixture, is mentioned on p. 2.

DISCUSSION OF RESULTS

The addition of 2-methylbutenal to citral in the presence of piperidine acetate resulted in the production of a dark-red, tasteless oil in which the odor of unchanged citral prevailed. When the material was subjected to molecular distillation after removal of the lower-boiling substances, about two-thirds of it could be distilled between 35 and 210°. A definite color sequence ranging from lemon-yellow, through orange, to dark-red, corresponded to the rising distilling temperatures of the various fractions. The fraction boiling at 75-95° (mainly 80-85°), was more closely examined. The yield of this fraction, considered as consisting of $C_{15}H_{22}O$ compounds, is about 40 per cent on the basis of 2-methylbutenal used. The substance is obtained as a dark-yellow oil. Its exact color tinge depends on the rate of distillation. The color fades upon exposure to air and darkens when the substance is kept in an atmosphere of nitrogen in sealed tubes, at room temperature. Its odor is similar to that of citral but less intense and refreshing.

The color of dihydrofarnesinal (reaction I) cannot be accurately predicted. Definite relations between color and unsaturation have been established only for symmetrical compounds containing chains of conjugated double bonds,[27] and the exact color equivalent of the aldehyde group is not yet known. The color of assymmetrical compounds shows considerable deviations from those predicted for symmetrical compounds on the basis of color-equiva-

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[27] See Kuhn and Grundmann, Ber., 70, 1323 (1937), and also previous publications by Kuhn and collaborators.

lence relations of the latter type of compounds. The absorption bands of assymmetrical compounds are shifted more towards the visible. In practice it is frequently impossible to remove highly colored impurities by distillation. As compared with Kuhn's β-ionylideneacetaldehyde, the dark-yellow material described here may appear to be somewhat too highly colored.

On the other hand the substance resisted all attempts at crystallization. It is miscible with all common organic solvents but less soluble in petroleum ether at low temperatures. It readily produces a violet color with Schiff's reagent, but reacts only slowly upon prolonged warming with Fehling's solution, probably due to its extreme insolubility in the reagent. With antimony trichloride in chloroform a red-brown coloration is obtained, indicating about three double bonds conjugated with the carbonyl group. With concentrated sulfuric and formic acids, dark-red and green colors were observed which immediately turned black. The molecular weight of the substance was found by the Rast method to be consistent with the molecular weight of $C_{15}H_{22}O$ compounds. Quantitative analysis of the material generally gave results that were somewhat high in hydrogen and definitely low in carbon content by about 0.8-1.00 per cent. The latter results are not surprising in view of the susceptibility of the material to oxygen. The deviation may be partly due to slight admixture of unchanged citral or a dimer of it. The lightest-colored portions of the fraction described here were obtained by molecular distillation of a part of the crude material which had been allowed to stand at room temperature for 8 weeks under carbon dioxide, and by steam distillation from a portion previously obtained by molecular distillation, but which had been kept in an atmosphere of nitrogen for 8 weeks and which had turned red. Both samples were obtained with

a dark-yellow color and showed the following analytical data:

Calc'd. for $C_{15}H_{22}O$: M.w. 218; C, 82.6 per cent; H, 10.1 per cent.
Found: From mol. dist., m.w. 205; C, 81.43; H, 10.5; from mol. and steam dist., m.w. 236; C, 81.53; H, 9.97.

The only solid derivative suitable for analysis was a small amount of a yellow semicarbazone obtained from the first-named portion. After five recrystallizations from aqueous and dry methanol, from which it is obtained as an oil crystallizing in the icebox, it began to darken at 135° and melted with decomposition at 143°. (Evac. tubes).

Calc'd. for $C_{16}ON_3H_{25}$: N_2, 15.25 per cent.
Found: 14.71 per cent.

Chromatographic development of the semicarbazone with benzene and petroleum ether on alumina showed one small yellow and one small pink zone, whereas the bulk of the material formed a wide yellow zone. The semicarbazone is fairly pure, and the observed melting point is probably close to the true one. It is not identical with the semicarbazone obtained from β-ionylideneacetaldehyde (white crystals, m.p. 193-95°).[28]

Attempts to oxidize various portions of the aldehyde material by means of silver oxide did not yield any crystalline acid. During the oxidation the odor of sour lemon was perceived, which persisted for several days.

In order to decide between a possible cyclic or chain configuration, the catalytic hydrogenation of the substance was studied. Hydrogenation at room temperature, using various concentrations of palladium and platinum oxide catalysts in different solvents generally resulted in the absorption of about three equivalents of hydrogen. Hydrogenation with palladium on barium sulfate at about

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[28] Kuhn and Morris, op. cit.

60° resulted in the absorption of 3.85 equivalents of hydrogen.

> 0.1384 grams of aldehyde. 1.75 grams of Pd on $BaSO_4$ (5 per cent). 605 cc. H_2 at 750 mm., 27° room temperature.

Provided that the carbonyl group has not been attacked to any appreciable extent, this would indicate the presence of four double bonds in the molecule and exclude cyclic configurations. This is partly supported by the color of the compound and by the coloration obtained with antimony trichloride in chloroform, which seem to exclude cyclic configuration that would arise from a Diels-Alder condensation of the aldehydes.[29] Although the results of the catalytic hydrogenation should be supported by the isolation and identification of the substances resulting from catalytic hydrogenation, such a procedure will be very difficult to carry out. The resulting material will consist of high-boiling oils which are hard to separate, particularly since they have several assymmetric carbon atoms which will probably give rise to various diastereoisomers. This latter factor also necessitates the use of larger amounts of material than were available in order to effect the preparation of solid derivatives for comparison with known substances. It is therefore not surprising that the hydrogenation product did not yield any solid derivatives (semicarbazones).

Ozonolysis without subsequent oxidation resulted in an aqueous distillate which gave the following tests:

Reagent	Reaction	Result
2,4-dinitrophenyl-hydrazine	Precipitate	Carbonyl compounds present
Schiff's reagent	Violet coloration	Aldehydes present
Fehling's solution	Decolorized upon warming	Aldehydes present

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[29] See page 8.

Reagent	Reaction	Result
Ammonia, acetic acid pine splinter	Pine splinter turns red when moistened with hydrochloric acid after boiling with reagent	γ-dicarbonyl compound present

In all probability the pyrrole test is due to the presence of γ-acetopropionylaldehyde which would result from the ozonolysis of I,[30] whereas the other two possible chain-condensation products of citral and 2-methylbutenal would result in 1-ketoglutaricaldehyde and 1,2-diketovaleraldehyde, respectively--compounds which would be expected to have a yellow color and, in the presence of hydrogen peroxide, to be unstable at the boiling point of water. No quantitative deductions as to the proportion of dihydrofarnesinal I in the investigated material could be based on either ozonolysis or an catalytic hydrogenation. Since cleavage products like γ-acetopropionylaldehyde (or the corresponding acid) cannot be obtained quantitatively by methods of oxidative degradation, only a quantitative determination of the amount of acetone formed could indicate the proportion of dihydrofarnesinal.

Alkaline degradation is unsuitable for the determination of structural configurations like dihydrofarnesinal, since its main product is tar.

Attempts to condense dihydrofarnesinal with 2-methylbutenal in the presence of piperidine acetate were less successful. The resulting dark-red oil, when subjected to molecular distillation, yielded starting material and higher boiling dark-red oils. The distillation ranges and molecular weights of these oils, determined by the Rast method, would be consistent with the presence of a compound of the composition $C_{20}H_{28}O$. However, in view of the apparent complexity of these materials, as revealed by quantitative

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[30] See page 3.

elementary analysis, their investigation was not pursued. The failure to obtain the desired condensation product may be ascribed to the following factors: In the first place, the desired condensation reaction presumably proceeds very slowly,[31, 32] so that the piperidine acetate catalyst will be "deactivated" by irreversible interaction with the aldehydes present before the action is completed. This necessitates a modification of the catalyst to render it less susceptible to the attack by aldehydes, e.g., by blocking the reactive positions in the piperidine ring as is partially effected in hexahydropicolinic acid (piperidinecarboxylic acid) or possibly by the use of proline[34] (2-pyrrolidinecarboxylic acid). In the second place, the temperatures required for the distillation of citrylidenedehydrocitral are probably already too high. A more efficient system of molecular distillation, or an entirely different method of separation, such as chromatographic absorption, must be applied.

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[31] This is probably the reason for the low yield of vitamin A_1 that was obtained by Kuhn and Morris. The subsequent Ponndorf reduction generally gives good yields.

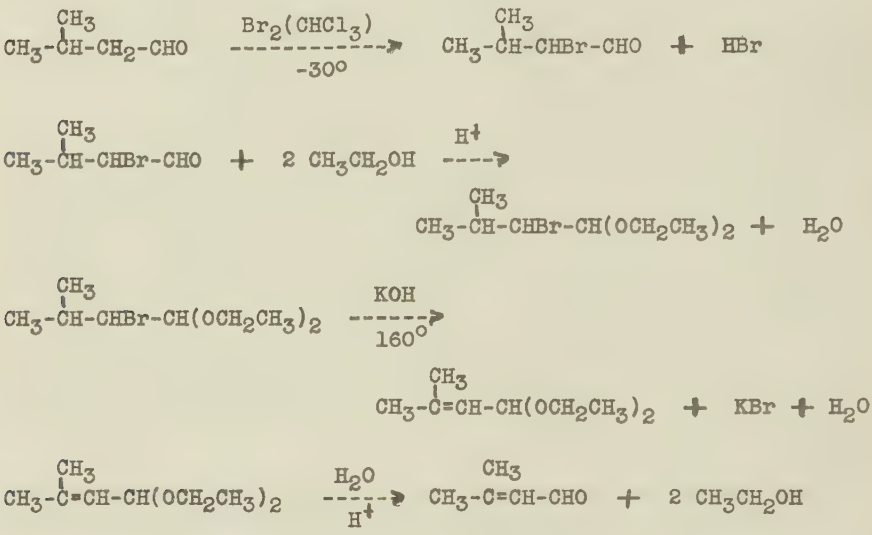
[32] The equilibrium may be unfavorable, too, but this may be overcome by the use of drying agents, like sodium sulfate, to remove water as it is formed. On the other hand, there is no a priori reason why the desired condensation should not proceed at all, since both dehydrocitral, whose "conjugation system" is isomeric with that of dihydrofarnesinal as well as farnesinal, readily yield carbonyl reaction compounds. Similarly, Kuhn has carried out the corresponding condensation with the isomeric β-ionylideneacetaldehyde (see page 6), and palmityl aldehyde has been isolated from the hydrogenation product of a mixture resulting from self-condensation of crotonaldehyde, i.e., hexadecaheptaenal is formed from four molecules of crotonaldehyde through octatrienal and dodecapentaenal.

[33] Interactions of two molecules of piperidine with one molecule of aldehyde to form compounds analogous to Schiff's bases are reversible in the presence of (acetic) acid; but the interaction of two molecules of aldehyde with one of the base results in compounds of unknown structure which distill with decomposition and from which piperidine cannot be regenerated.

[34] Preliminary trials showed that proline promotes aldol condensations.

EXPERIMENTAL

2-Methylbutenal was prepared from isovaleraldehyde according to the method of Fischer and Löwenberg:[35]



Isovaleraldehyde was obtained from isoamylalcohol b.p. 130-32° by oxidation with air at 240°, in the presence of finely divided silver(asbestos); yield, 65 per cent. The yields of the above reactions were as follows:

Acetal of α-bromisovaleraldehyde	b.p. 87-91°/15	81 per cent
Acetal of 2-methylbutenal	b.p. 87-88°/60	75 per cent
2-Methylbutenal	b.p. 63-65°/60	66 per cent

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[35] Fischer and Löwenberg, Ann., 494, 272 (1932). See also Idem., Ber., 64, 30 (1931).

[36] See Mourεu, Compt. rend., 170, 258 (1920).

The hydrolysis of the unsaturated acetal was modified when difficulties arose in the use of calcium chloride. A solution of sodium sulfate in water was used for the hydrolysis after the addition of saturated tartaric acid solution. The water layer was extracted with thiophene-free benzene (extractions with chloroform are still more convenient), the organic liquids were united, dried over sodium sulfate, and distilled in an inert atmosphere through a 30 cm. column of the Podbielniak type. On dry ice the aldehyde can be kept in corked containers practically unchanged. The unsaturated acetal can be conveniently kept at room temperature.

Condensation of Citral with 2-Methylbutenal

In order to effect this condensation, citral, as the more conveniently available material, was kept in large excess and 2-methylbutenal was slowly added to it at room temperature. Citral (Eastman) was redistilled from a Claisen flask in a stream of pure nitrogen. The first fraction was always colorless, the desired fraction sometimes slightly yellow. Piperidine acetate was prepared by adding slowly an equivalent amount of glacial acetic acid to piperidine in absolute ether. Eastman piperidine was used without further purification.[37]

For aldol condensations with 2-methylbutenal in which one reagent was gradually added to the other, a special reaction vessel was used. Two round-bottomed flasks are connected by a U-tube (about 45° angle), with a capillary tube pointing upward, and sealed in one arm. The reagents are introduced through side-arms attached to the U-tube near the flasks. The reagent to remain in excess with the catalyst, is placed in the larger flask near the

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[37]The purity of the piperidine is of great importance for aldol condensations involving unsaturated aldehydes. See Kuhn, J. Chem. Soc., London, 608 (1938).

capillary. The side-arms are sealed off, the system is evacuated with a mercury pump, while both flasks are cooled in dry ice-acetone (the 2-methylbutenal flask preferably immersed in liquid nitrogen), and the whole system is sealed off. The addition is carried out by repeated tipping over of the U-tube to allow the reagent to flow through the capillary into the other flask. The capillary permits a better control of the amounts added. Whenever the addition was extended over several days, the flask containing the catalyst was kept on dry ice overnight in order to minimize side-reactions. After completion of the reaction, the system is opened in an atmosphere of carbon dioxide. The contents are distilled (water pump vacuum) from a Claisen flask to remove low-boiling material, including citral, Considerable foaming occurs and necessitates careful regulation of the distillation. The residue is kept under carbon dioxide in the dark and is distilled in portions with the Hickman still (the scheme of the still is shown at the end of the paper). Generally the molecular distillation proceeded at a rate of about one drop per minute. The Hickman still was operated by means of an electrically heated air-bath. In order to obtain an optimal vacuum, wide glass tubing was used and as few as possible attachments made. The top of the still is cooled by dry ice, the receiver being immersed in ice water.

Two hundred grams of freshly redistilled citral was added to 8.5 grams of piperidine acetate, 4 grams of piperidine in about 12-20 cc. of absolute alcohol. The mixture (cooled to -78°) slowly turns reddish. Fifty-two grams of 2-methylbutenal was placed in the other flask which was cooled likewise, and the system was evacuated and sealed off. Addition was started the following day in portions of about 1/2 cc., which were added at intervals of 15 to 25 minutes, over a period of three days. In the beginning of

the addition slight warming of the reaction mixture is observed. About 50 cc. of liquid was collected up to 37°/25 mm. The distillate was not examined; the odor of 2-methylbutenal was perceived. Other low-boiling substances in the original mixture were water, alcohol, piperidine, and acetic acid (ethyl acetate). In order to remove uncombined citral completely, the oil-bath temperature had to be raised to 170°. A residue of about 210 cc. remaining in the Claisen flask, was kept in the dark under carbon dioxide and was distilled in portions from the Hickman still. A few drops of high-boiling ligroin sufficed to wash down material remaining in the pipette used for the transfer, as well as from the bend of the still. The solvent was removed by gradually reducing the pressure by means of a motor-pump. With low-boiling ligroin spattering results, which has to be carefully avoided. For this purpose degassing was effected by heating the still gradually to about 65° at 20 mm. pressure, rather than lowering the pressure at room temperature. After removal of the solvent and degassing, the system is evacuated with the mercury pump; during the distillation the top of the still is cooled with dry ice, and its outlet to the pump is cooled by a stream of air.

Semicarbazone

Two tenths grams of semicarbazide hydrochloride and 0.2 grams of potassium acetate were dissolved in the minimum of water, and about 0.2 grams of aldehyde and enough alcohol were added to the aqueous solution to dissolve the aldehyde. The solution was removed from the precipitate of potassium chloride and allowed to stand at room temperature for 4 days. The solvent was removed (water pump vacuum) and the remaining material crystallized from methanol.

Ozonization

Two grams of aldehyde in 30 cc. of carbon tetrachloride were treated with ozonized oxygen for 12 hours, and then the solvent was decanted from a brown precipitate. The precipitate was warmed with water and finally refluxed with water for one hour. A part of the brown material did not go into solution, indicating that overozonization had occurred. Half of the water solution was distilled and the distillate tested.[38]

Catalytic Hydrogenation

0.1384 grams of aldehyde were dissolved in about 12 cc. of glacial acetic acid and shaken with 1.75 grams of palladium on barium sulfate (about 5 per cent palladium) at 60° (air bath) for one half hour. About two thirds of the hydrogen absorption was completed after 6 minutes.[39]

Attempts to Condense Dihydrofarnesinal with 2-Methylbutenal

In one attempt, dihydrofarnesinal, as the more valuable material was added slowly at room temperature to 2-methylbutenal in an atmosphere of carbon dioxide. Seven and five tenths grams of dihydrofarnesinal were added to 9.5 grams of 2-methylbutenal containing about 0.6 grams of piperidine acetate, and about 0.3 grams of piperidine in a little alcohol in the presence of sodium sulfate. Upon each addition, save for that of the last part of the material, the mixture warmed up distinctly. The addition took eight hours. The solution was then distilled from a Claisen flask (water pump vacuum, stream of carbon dioxide) while the oil-bath temperature was raised to about 115°. The residue was subjected

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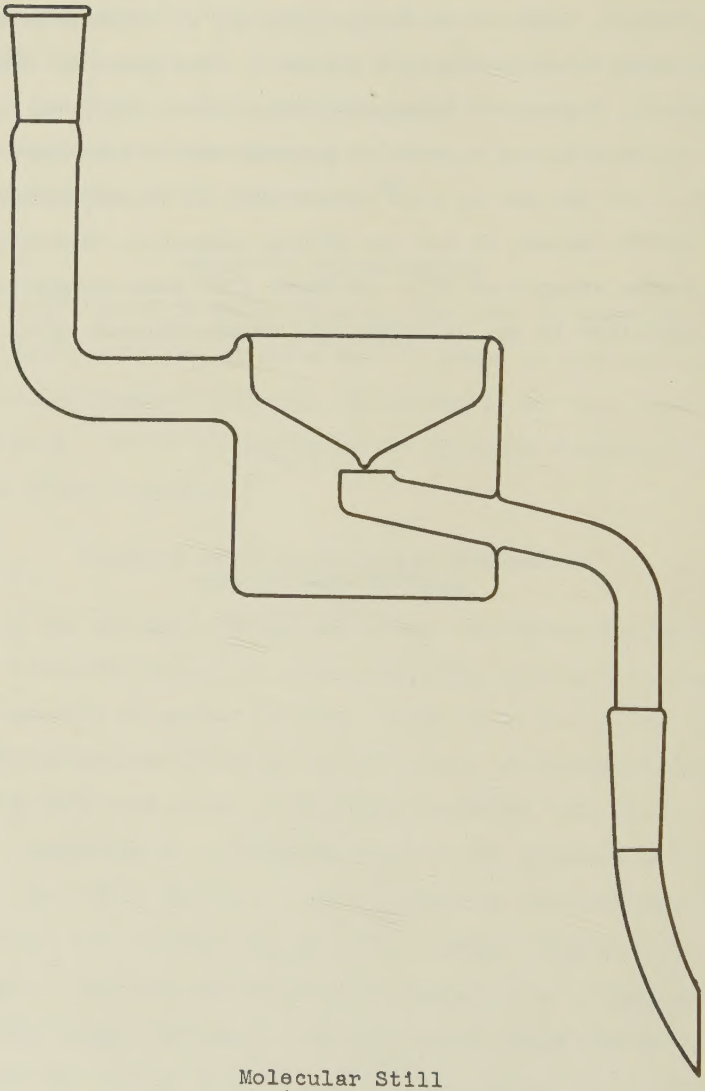
[38] See page 15.

[39] See page 14.

to molecular distillation. Two thirds of it distilled between 35 and 210° (air bath).

In another sample run, both aldehydes were allowed to react at room temperature in the presence of piperidine acetate, with glacial acetic acid as a solvent. Five grams of dihydrofarnesinal, 7 grams of 2-methylbutenal, about 0.2 grams of piperidine (5 drops), and 2 grams of glacial acetic acid were allowed to stand for one day at room temperature in an atmosphere of nitrogen. After removal of the low boiling material, distillation in high vacuum started at 35°. At about 170° some orange-red crystals were deposited in the delivery tube of the Hickman still.



Molecular Still
(Hickman)